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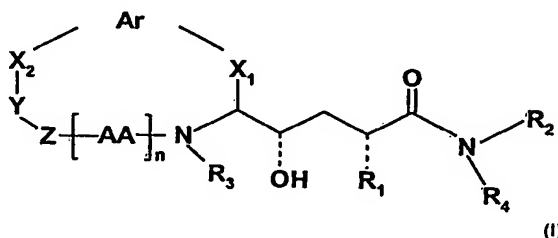
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(54) Title: **MACROCYCLIC COMPOUNDS HAVING ASPARTIC PROTEASE INHIBITING ACTIVITY AND PHARMACEUTICAL USES THEREOF**



(I)

hydrogen or (C₁₋₄)alkyl, X₁ is CH₂, X₂ is CH₂, O, S, CO, COO, OCO, NHCO, CONH, or NR, R being hydrogen or (C₁₋₄)alkyl, Y is (C₁₋₈)alkylen or (C₁₋₈)alkylenoxy(C₁₋₆)alkylen, (C₁₋₈)alkenylen or (C₁₋₈)alkenylenoxy(C₁₋₆)alkylen, Ar is a phenyl ring optionally mono- di or trisubstituted by, independently, hydroxy or halogen, whereby X₁, and X₂ are in meta or para position to each other, and either Z is CO, AA is a natural or unnatural alpha-amino-acid, and n is 0 or 1, or Z is SO₂, AA is an optionally substituted ethylencarbonyl group (derived from a natural or unnatural alpha-amino acid by replacement of the nitrogen by a methylen group), and n is 1; processes for the preparation of these compounds; pharmaceutical compositions and combinations comprising the same; and their use in the treatment of neurological and vascular disorders related to beta-amyloid generation and/or aggregation.

(57) Abstract: The present invention relates to macrocyclic compounds of formula (I), wherein R₁, is (C₁₋₈)alkyl, (C₁₋₄)alkoxy(C₁₋₄)alkyl, hydroxy(C₁₋₆)alkyl, (C₁₋₄)alkylthio(C₁₋₄)alkyl, (C₁₋₆)alkenyl, (C₃₋₇)cycloalkyl, (C₃₋₇)cycloalkyl(C₁₋₄)alkyl, piperidiny or pyrrolidinyl, R₂ and R₄, independently, are hydrogen or optionally substituted (C₁₋₈)alkyl, (C₃₋₇) cycloalkyl, (C₃₋₇)cycloalkyl(C₁₋₄)alkyl, aryl, aryl(C₁₋₄)alkyl, heteroaryl or heteroaryl(C₁₋₄) alkyl, or R₂ and R₄, together with the nitrogen to which they are attached, form an optionally substituted piperidino, pyrrolidinyl, morpholino or piperazinyl group, R₃ is (C₁₋₈)alkylen or (C₁₋₈)alkylenoxy(C₁₋₆)alkylen, (C₁₋₈)alkenylen or (C₁₋₈)alkenylenoxy(C₁₋₆)alkylen, Ar is a phenyl ring optionally mono- di or trisubstituted by, independently, hydroxy or halogen, whereby X₁, and X₂ are in meta or para position to each other, and either Z is CO, AA is a natural or unnatural alpha-amino-acid, and n is 0 or 1, or Z is SO₂, AA is an optionally substituted ethylencarbonyl group (derived from a natural or unnatural alpha-amino acid by replacement of the nitrogen by a methylen group), and n is 1; processes for the preparation of these compounds; pharmaceutical compositions and combinations comprising the same; and their use in the treatment of neurological and vascular disorders related to beta-amyloid generation and/or aggregation.